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Constipation: Beyond the Old Paradigms

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Keywords

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Key Points

- Although the majority of children with constipation respond to conventional treatment, symptoms will persist in a minority. Recent advancements offer promise in the management of these children.
- Identifying a rectal evacuation disorder or colonic motility disorder by performing anorectal and colonic manometry testing can guide subsequent management.
- Novel pharmacological treatments used in adults with constipation are beginning to be used in children with promising results.
- Biofeedback therapy and anal sphincter botulinum toxin injection can be considered for the child with a rectal evacuation disorder.
- Surgical management of constipation includes the use of antegrade continence enemas, sacral nerve stimulation, colonic resection, and stoma creation.

SYNOPSIS

Constipation is a common problem in children. Although most children respond to conventional treatment, symptoms will persist in a minority. For children with refractory constipation, anorectal and colonic manometry testing can identify a rectal evacuation disorder or colonic motility disorder and guide subsequent management. Novel medications used in adults with constipation are beginning to be used in children with promising results. Biofeedback therapy and anal sphincter botulinum toxin injection can be considered for the child with a rectal evacuation disorder. Surgical management of constipation includes the use of antegrade continence enemas, sacral nerve stimulation, and colonic resection.

1. INTRODUCTION

Constipation is commonly encountered in children and can result from a number of medical conditions, ranging from congenital abnormalities to metabolic disorders. However, most children with constipation do not have any underlying medical condition causing their constipation and therefore have functional constipation (FC) (1). The Rome criteria are the most widely used diagnostic criteria for FC, and the recently released Rome IV criteria define FC as experiencing two or more of the following at least once a week over the past month (2):

1. Two or fewer bowel movements per week
2. At least one episode of fecal incontinence per week
3. History of retentive posturing or excessive volitional stool retention
4. History of hard or painful bowel movements
5. Presence of a large fecal mass in the rectum
6. History of large diameter stools that can obstruct the toilet

Pediatric population-based studies on constipation from around the world describe a prevalence ranging from 0.7% to 29.6% with a

median of 12% (3). The cost associated with the care of children with constipation is substantial. Using data from 2003-2004, it was estimated that medical care for children with constipation accounted for an additional $3.9 billion in medical costs per year in the United States (4). This figure is likely now significantly higher, particularly as both the number of hospitalizations for children with constipation and the mean cost of each hospitalization in the United States have been steadily increasing (5). However, despite how common constipation is in children, our understanding of the prognosis of a child with FC is limited. The studies available are few and heterogeneous, but one review found that after 5 to 10 years of follow up, only 56% of children had recovered and were no longer taking laxatives. Children who were treated by a specialist had a higher success rate, but over a quarter continued to have symptoms requiring laxative treatment at follow up (6).

The North American and European societies of pediatric gastroenterology recently put forth evidence-based recommendations on the treatment of FC. Conventional treatment of FC includes education of the child and family, toilet training, and oral medications, including osmotic and stimulant laxatives. If the child's symptoms persist, assessment of treatment adherence and adjustment of laxative

treatment may be needed (1). However, a proportion of children will have symptoms despite conventional treatment, and the management of this population can be challenging and varies widely among providers and institutions (7).

For these children, the treatment paradigm is evolving. In this review, we will summarize recent advancements in the evaluation and treatment of children with FC and discuss their clinical applications, particularly to children with continued symptoms despite conventional treatment. Identifying the mechanisms contributing to a child's presentation can allow for more personalized and effective management.

2. EVALUATION

The diagnosis of FC is a clinical one made using the Rome criteria. However, further evaluation may still be needed after establishing the diagnosis of FC, particularly for the child with refractory symptoms. The symptoms associated with FC can result from a number of underlying mechanisms. If a child's symptoms do not respond to conventional treatment, testing may be able to identify contributing factors for that individual patient, allowing a better understanding of

the child’s constipation and potentially guiding subsequent treatment (1). This evaluation should begin by ensuring that a thorough history and physical examination have been completed.

Although this review will discuss a number of diagnostic tests, it is important to remember that the majority of children with FC will not need any of them. The primary role of a thorough history and physical examination is to exclude an underlying organic disorder, but the history may also guide the provider’s management (1). For example, a report of prolonged straining to pass soft stool could increase one’s suspicion for pelvic floor dyssynergia. The history should also include an assessment of the impact of a child’s symptoms on daily functioning and quality of life. For the older child with daily retentive fecal incontinence who is wearing diapers and has withdrawn from school, one’s treatment plan would be more aggressive and include a plan to return to school.

For those who continue to have symptoms despite optimal conventional treatment, diagnostic testing may be able to identify a responsible mechanism that would guide subsequent treatment. In a broad sense, evaluation would aim to identify whether the child’s

constipation is secondary to a rectal evacuation disorder, a colonic motility disorder, or potentially both concurrently.

2.1 Evaluation for a rectal evacuation disorder

Anorectal manometry

Anorectal manometry testing involves assessment of the neuromuscular function of the anus and rectum by using a manometric catheter placed through the anal canal and into the rectum. Anorectal manometry is the most commonly performed gastrointestinal motility test in children and has become more widely available over time. The North American societies for neurogastroenterology and motility and pediatric gastroenterology recently published a consensus document on anorectal and colonic manometry testing (8).

The catheter used for anorectal manometry has evolved with time, from standard water-perfused catheters to solid-state high-resolution catheters to three-dimensional high-definition catheters that allow for dynamic imaging of the anal canal (**Figure 1**). Most of the experience with anorectal manometry testing in children thus far has been using water-perfused and solid-state catheters, and the utility of three-dimensional catheters in pediatrics, although promising, is still unclear

(9). For the cooperative child, anorectal manometry testing involves measurement of resting anal pressure and the length of the anal canal, evaluation of squeeze and bear down (or push) mechanisms, and evaluation of rectal sensation and for a recto-anal inhibitory reflex with progressive rectal balloon inflation. Balloon expulsion testing can be informative as well (8). A paradoxical increase in external anal sphincter pressure during the bear down maneuver can be suggestive of an increase in anal pressure during attempts to defecate and pelvic floor dyssynergia (10).

For the younger or uncooperative child, anorectal manometry testing can be attempted under sedation. It is important to recognize that even for older children, the test can be associated with significant anxiety in both the child and parent (11). Sedation limits the test to assessment of resting anal pressure and evaluation for a recto-anal inhibitory reflex, and anesthetic agents like propofol can decrease the ability to measure a useful resting anal pressure (12). The primary utility in performing an anorectal manometry test under sedation is in evaluating for Hirschsprung’s disease or anal sphincter achalasia, which should be suspected if the recto-anal inhibitory reflux is absent (8).

Defecography

Defecography is a radiologic test used to assess the pelvic floor during the act of defecation, and can be useful in identifying pelvic floor dyssynergia and also structural abnormalities like rectocele or rectal prolapse. Experience with defecography in children is limited, but the test is safe and generally well-tolerated in children older than 4-5 years of age (13, 14). A small study of children with defecation disorders evaluated by fluoroscopic defecography reported that results directly influenced subsequent treatment in 67% of their cohort (13). However, defecography involves radiation exposure and experience in adults has raised concerns regarding interobserver bias and variable methodology among centers (15).

2.2 Evaluation for a colonic motility disorder

Colonic transit testing

Measurement of colonic transit time can be helpful in the evaluation of the child with refractory FC. The most commonly used method of colonic transit testing is by using radiopaque markers. After ingestion, the position of these markers in the colon is evaluated by abdominal radiograph(s) (**Figure 2**). While inexpensive and simple to perform, test protocols and interpretative methods vary among institutions (16,

17). One of the more commonly used methods involves ingestion of a capsule containing a set number of markers on three consecutive days. This is followed by an abdominal radiograph on the fourth day and in some cases another radiograph on the seventh day. Using skeletal landmarks to divide the colon into segments, both segmental and total colonic transit time can be calculated and compared to normative data (16).

Colonic scintigraphy involves measuring the transit of an ingested radioisotope through the colon. One study in children showed that colonic scintigraphy was well-tolerated and demonstrated fair agreement with colonic manometry in differentiating between normal transit, delay in the distal colon, and colonic inertia (18). Wireless pH-motility capsule testing has been used to measure colonic transit time in adults, and measurements correlate well with results of radiopaque marker testing (19). Wireless pH-motility capsule testing has been shown to be safe and well-tolerated in children, but its use for measurement of colonic transit time in children remains untested (20). Normal colonic transit and prompt evacuation of radiopaque markers or radioisotope in a child with frequent fecal incontinence should raise concern for non-retentive fecal incontinence (1). Prompt transit to the rectum with retention of markers or radioisotope may suggest of a

rectal evacuation disorder. Slow colonic transit in a child with refractory FC would benefit from assessment of segmental colonic function by colonic manometry evaluation when available.

Colonic manometry

Colonic manometry testing involves assessment of colonic motor activity by using a manometry catheter placed in the lumen of the colon. Similar to the catheters used for anorectal manometry, the catheters used for colonic manometry have also evolved from primarily water-perfused catheters to solid-state high-resolution catheters (21). Catheter placement is generally performed under general anesthesia during colonoscopy or with fluoroscopic guidance. Some centers use an endoscopic clip to attach the distal tip of the catheter to the colonic mucosa to reduce migration during the study (**Figure 3**) (8). There is evidence that recent anesthesia can affect subsequent colonic manometry results, although the length of time needed for this effect to cease is unclear (22, 23).

Once the catheter is in place and time has been given for recovery after anesthesia, the colonic manometry test begins. Although testing protocols vary among providers and institutions, testing generally

begins with assessment of colonic activity while fasting. This is followed by a meal and assessment for a gastrocolic response, characterized by a physiologic increase in colonic contractions and tone after a meal. Series of high-amplitude propagating contractions can occur in all phases of the study, but can be seen as part of the gastrocolic response. In some cases (i.e. when high-amplitude propagating contractions are absent or limited after the meal), this is followed by provocative testing to assess the colonic response to drug challenge, most commonly by evaluating for high-amplitude propagating contractions after administration of bisacodyl (**Figure 4**) (8).

For the child with refractory FC, colonic manometry testing can identify a colonic motility disorder. Although there is growing evidence that colonic motor patterns observed during manometry testing other than high-amplitude propagating contractions are likely to be clinically meaningful, the presence of these contractions remains the most recognizable and clinically significant portion of the test (24, 25). Absence of high-amplitude propagating contractions throughout the colon suggests colonic inertia. Propagation that terminates prematurely (i.e. before reaching the distal sigmoid colon) suggests segmental colonic dysmotility. By correlating manometry results with

an abdominal radiograph taken after catheter placement, the provider can estimate the length of dysmotile colon, which can be helpful if surgical resection is needed (8, 26). Normal colonic manometry is associated with an improved response to antegrade continence enema (ACE) treatment (27-30).

However, the utility of colonic manometry is not limited to the measurement of colonic contractile activity alone. Clinical observation of the patient during the study can be revealing as well. Children with FC who deny the urge to defecate will often demonstrate that they do sense high-amplitude propagating contractions through non-verbal communication like grimacing or posturing. Children may also demonstrate evidence of volitional stool retention. For these children, it may be helpful for them to recognize that the sensation they felt at the time of propagating contractions should prompt them to have a bowel movement (31).

3. TREATMENT

Treatment of the child with FC begins with education of the child and family, toilet training, and oral medications, including traditional osmotic and stimulant laxatives. As discussed earlier, conventional

treatment will be sufficient for the majority of children with FC (1). Treatment options for children with symptoms refractory to optimal conventional treatment have traditionally been limited, but recent advancements offer promise. A number of novel pharmacological treatments have emerged for adults with constipation and constipation-predominant irritable bowel syndrome that are beginning to be used in the pediatric population. For the child with FC and an identified rectal evacuation disorder and/or colonic motility disorder, non-pharmacological treatment options beyond conventional treatment can be chosen based on the mechanisms contributing to the child's presentation.

3.1 Novel pharmacological treatments

Traditional pharmacological treatment for children with FC generally begins with use of osmotic laxatives like polyethylene glycol, followed by use of stimulant laxatives or lubricants if symptoms persist (17). Evidence-based recommendations on laxative treatment for children with FC have been published (**Table 1**) (1). However, newer pharmacological treatments have been used successfully in adults with constipation and constipation-predominant irritable bowel syndrome. Experience with these medications remains limited in children with FC but is growing with time.

Lubiprostone is a prostaglandin E1 derivative that promotes intestinal fluid secretion by acting on the type 2 chloride channel, softening stool and promoting intestinal motility in response to luminal distention (17). Lubiprostone is approved in the United States for treatment of chronic idiopathic constipation in adults and irritable bowel syndrome with constipation in adult women (32). Several randomized, controlled studies have demonstrated the efficacy and safety of lubiprostone in adults with constipation (33-35). In a multicenter, open-label study of children with FC, lubiprostone led to a significant increase in bowel movement frequency and was generally well tolerated, with nausea, vomiting, and diarrhea as the most common adverse events (32). A randomized, controlled trial in children is underway (17).

Linaclotide is a peptide agonist of the intestinal guanylate cyclase-C receptor, promoting intestinal fluid secretion. Linaclotide not only softens stool and promotes intestinal motility, but also reduces visceral sensitivity in animal models. Linaclotide is approved in the United States for treatment of chronic intestinal constipation in adults and irritable bowel syndrome with constipation in adults (36). Randomized, controlled studies in adults have demonstrated significant improvement in bowel movement frequency and abdominal pain.

Treatment was generally well-tolerated, with diarrhea as the most common adverse event (36-38). No studies have yet been completed in children.

Prucalopride is a highly selective 5-HT4 serotonergic agent that increases acetylcholine release and subsequently increases intestinal motility, particularly in the lower gastrointestinal tract (39). Multiple randomized, controlled studies in adults with chronic idiopathic constipation have demonstrated significant improvement in bowel movement frequency (40-42). In an initial open-label study of children with FC, prucalopride led to improvements in bowel movement frequency, fecal incontinence, and stool consistency. Prucalopride was generally well-tolerated in children (43). However, a multicenter, randomized, controlled study did not find any difference in clinical response or perceived benefit when compared to placebo (44).

3.2 Treatment of a rectal evacuation disorder

Biofeedback therapy

The purpose of biofeedback therapy is to restore a normal pattern of defecation using visual and verbal feedback techniques. For the child with pelvic floor dyssynergia, this involves training the child to relax

the external anal sphincter while increasing abdominal pressure during attempts to defecate. Visual feedback is provided either by placing an anorectal manometry catheter to demonstrate abdominal and anal pressures or by applying surface electromyography leads externally. The duration of biofeedback therapy (i.e. number of training sessions required) varies depending on the child's response. Although the North American and European societies for neurogastroenterology and motility recommend biofeedback therapy for adults with pelvic floor dyssynergia based on high-quality evidence, the efficacy of biofeedback therapy in children for the same indication is less clear and routine treatment with biofeedback therapy was not recommended (45).

Studies of children with FC treated with biofeedback therapy have shown variable results. Although some studies have found clinical improvement in as many as 90% of children with FC treated with biofeedback therapy, a number of controlled studies have not found any significant long-term improvement over conventional treatment (1, 45-47). Two large randomized, controlled studies did not find biofeedback therapy to be helpful compared to conventional treatment (education, toilet training, and laxatives) or in addition to conventional treatment (48, 49). However, a recent randomized, controlled study

evaluating the addition of biofeedback therapy to conventional treatment did demonstrate a significant advantage in symptomatic improvement and ability to discontinue laxative treatment (46). Interestingly, studies have not demonstrated an association between improvement and normalization of defecation dynamics based on anorectal manometry (47, 49).

The role that biofeedback therapy plays in the management of a child with FC therefore remains unclear. For the child with a rectal evacuation disorder and persistent symptoms despite optimal conventional treatment, biofeedback therapy is an option that can be considered, particularly given its lack of adverse effects. However, biofeedback therapy is only feasible in an older, cooperative child, and the training itself is labor-intensive and requires a practitioner with specialized training (45).

Anal sphincter botulinum toxin injection

Injection of botulinum toxin into the anal sphincter has been used for children with impaired rectal evacuation secondary to Hirschsprung's disease, anal sphincter achalasia, or anal fissure, generally with good response (50-55). Injection is performed under sedation, often by

dividing the administered toxin into the four quadrants of the internal anal sphincter. Injection is typically well-tolerated, with transient fecal incontinence, rectal pain, and pelvic muscle paresis as potential side effects (52, 54).

Evidence of the efficacy of anal sphincter botulinum toxin injection for children with FC and a normal recto-anal inhibitory reflex remains limited. A randomized study of children with refractory FC found that improvement after anal sphincter botulinum toxin was comparable to internal anal sphincter myectomy. Children who had low anal resting pressures were excluded, but the cohort included children with normal and elevated resting pressures (56). In a cohort study that included children who had a "high-threshold recto-anal inhibitory reflex," investigators reported symptomatic improvement after injection (57). Interestingly, in a recent survey of pediatric gastroenterologists and surgeons, over half of respondents reported that they would use anal sphincter botulinum toxin injection to treat a child with refractory FC who had an intact recto-anal inhibitory reflex and an increased resting anal pressure, suggesting that the use of botulinum toxin injection for treatment of FC may be more common than the literature suggests (7). Further studies are needed to clarify the role of anal sphincter

botulinum toxin injection in the treatment of children with FC and a rectal evacuation disorder.

3.3 Surgical treatment of functional constipation

Antegrade continence enemas (ACE)

ACE treatment involves the administration of an enema into the proximal colon through surgical creation of an appendicostomy or cecostomy. The choice of procedure is based in part on patient and surgeon preference. While appendicostomy creation offers some cosmetic advantage with the ability to hide the site at the umbilicus (with access obtained by cannulation), a minority of children can experience stricture formation. Cecostomy creation requires placement of a tube used for access (26). Complications of appendicostomy and cecostomy are not uncommon, particularly minor complications like pain with catheterization, skin irritation or granulomata, stomal leakage, and stomal stenosis (58).

Although a number of case series describing outcomes of ACE treatment have been published over the past two decades, few have been prospective (58). Studies have also been variable in both the definition of successful treatment and rate of success (59). A review of

the existing literature found that positive outcomes were been reported in 82% of children treated with ACE, but resolution of symptoms allowing appendicostomy or cecostomy closure was reported only in 9.5% (58). A larger, prospective cohort study that included children with both functional and organic causes of constipation reported that 93% of children had a positive response, and that approximately a quarter of children were no longer using ACE after a mean follow up duration of 5.5 years. Children with FC were more likely to no longer require ACE treatment (60). A recent retrospective review supports the finding that children with FC may be more likely to discontinue ACE treatment, estimating that after five years of ACE treatment, approximately a third of children would have their ostomy closed (61).

Colonic manometry may play a role in predicting a child's response to ACE treatment. Several studies have found that normal colonic manometry prior to ACE treatment is associated with a better response to ACE treatment (27, 28). In children with colonic dysmotility prior to ACE treatment, repeat colonic manometry after ACE treatment often shows improvement in colonic motility (62). A more recent retrospective review of children with FC who completed colonic manometry testing before and after ACE treatment initiation reported

that the baseline manometry was not predictive of outcome, but high-amplitude propagating contractions on repeat manometry after ACE treatment was associated with a decreased need for ACE treatment (29).

Neurostimulation

Over the last two decades, there has been increasing interest in the use of neurostimulation for treatment of children with refractory FC as an alternative to more invasive surgical procedures. Although pediatric experience with neurostimulation for gastrointestinal disorders remains limited, several modalities have shown promise and warrant further investigation.

Sacral nerve stimulation (SNS) is perhaps the most established form of neurostimulation used in children with defecation disorders. SNS involves the delivery of low-amplitude electrical stimulation to the sacral nerve root via an electrode placed in the sacral foramen (**Figure 5**). This electrode is connected to a pulse generator and battery that may remain external to the child during an initial temporary stimulation trial before permanent implantation into a subcutaneous pocket in the buttock (63). The initial reports of SNS for treatment of

children with bladder dysfunction described improvement in not only urinary symptoms, but constipation and fecal incontinence as well (64-66). Two institutions have recently published long-term outcomes of SNS treatment for children with severe constipation. In one study of females with FC, significant improvement in constipation continued after a median follow up of 22 months. However, 56% were considered not to have had a successful response to SNS based on bowel movement frequency (67). We recently described the two-year outcomes of a group of children treated with SNS for constipation, of which the majority had refractory FC. Although bowel movement frequency did not change significantly, durable improvement was seen in fecal incontinence and associated quality of life. Nearly all families surveyed reported health-related benefit (68).

The role of SNS in relation to other surgical treatment options for FC (like ACE or colonic resection) remains unclear. In a study of children with continued constipation despite ACE treatment, SNS allowed for a steady decrease in ACE usage. At a median of 18 months of follow up, 45% had not only discontinued ACE usage, but had undergone appendicostomy or cecostomy closure. SNS can be considered for the child with FC who has persistent symptoms despite ACE treatment (69). In a recent study comparing children with FC treated with ACE or

SNS, it appears that ACE leads to greater improvement in bowel movement frequency and abdominal pain, but SNS may lead to greater improvement in fecal incontinence (70). This is consistent with the adult experience with SNS, where randomized, controlled studies have demonstrated significant improvement in adults with fecal incontinence but not FC (71, 72).

When considering SNS treatment, it is important to recognize that the likelihood of complications requiring further surgery is not inconsequential. In the largest cohort of children treated with SNS, 49% of children experienced complications requiring further surgery (73). In addition to the two procedures required for SNS initiation, a proportion of children will require lead revision, device removal, or device replacement, most often performed because of lead displacement or malfunction, local pain or numbness, and local infection (67, 68). Unfortunately, attempts to identify factors predictive of complications after SNS have not been successful (74).

Non-invasive forms of neurostimulation for FC are therefore needed. Abdominal transcutaneous electrical stimulation (TES) is the best-studied non-invasive modality, and involves placement of two surface electrodes on the anterior abdomen at the level of the umbilicus and

two on the lower back at the level of the upper lumbar spine. These electrodes are used to generate two sinusoidal currents that cross within the abdomen and apply interferential electrical current to the abdomen at an intensity below the motor threshold (75, 76). Preliminary studies demonstrated improvement in constipation, but a recent review reported that results of a randomized, controlled study did not demonstrate significant differences in clinical response between abdominal TES and sham stimulation (77). Nonetheless, given the advantages conferred by the non-invasive nature of abdominal TES, which are particularly relevant to the pediatric population, further investigation is needed. A recent cohort study demonstrated that home-based abdominal TES was feasible for children with FC and led to significant improvement in bowel movement frequency, fecal incontinence, and abdominal pain (78).

Colonic resection

For the child with FC and continued severe, debilitating symptoms despite optimal medical management, colonic resection may be beneficial. Careful evaluation and consideration is needed prior to surgery, particularly as the available literature in children remains limited and specific indications for surgery unclear. A variety of procedures have been described, with the general aim of removing

dilated, dysmotile colon thought to be responsible for the child's persistent symptoms (26, 58). Colonic manometry, particularly in cases when manometry demonstrates segmental dysmotility, may be useful to guide surgical decision-making (7, 26). Colonic resection can be combined with creation of an appendicostomy to allow for administration of ACE postoperatively, which can decrease the need for oral laxatives and limit postoperative fecal incontinence (79).

Stoma formation and bowel diversion

Temporary or permanent stoma formation and bowel diversion may be needed in certain situations. The literature on this topic is sparse and of limited quality. Based on small case series, almost half of children treated with stoma formation are able to undergo delayed restoration of intestinal continuity with good outcomes (26, 58). Stoma formation, specifically by creation of an ileostomy, may be beneficial for the young child (<3 years of age) with colonic manometry testing demonstrating diffuse colonic dysmotility, particularly in those with resulting failure to thrive. In these children, evaluation for chronic intestinal pseudo-obstruction, which almost invariably involves the small bowel as well, is critical as a positive diagnosis would have therapeutic and prognostic implications (26).

4. CONCLUSION

The majority of children with constipation will respond to education, toilet training, and laxatives and will not require any testing aside from a thoughtful history and physical exam. However, for the minority of children who continue to have symptoms despite conventional treatment, advancements over the past decade promise to elevate their management beyond the old paradigms. Constipation is the end result of a number of potential contributing mechanisms, and diagnostic testing to identify the mechanism relevant to the individual child can guide subsequent treatment. Manometry testing is becoming more precise and results more meaningful. New medications will undoubtedly soon be available for children with refractory constipation. Measurement of anorectal function and colonic motility can inform the use of an array of non-pharmacological treatment options, including biofeedback therapy, anal sphincter botulinum toxin injection, ACE treatment, neurostimulation, and colonic resection.

FIGURES AND TABLES

Figure 1: Anorectal manometry performed using a three-dimensional high-definition catheter allows for dynamic recreation of the anal canal.

Figure 2: An abdominal x-ray taken several days after ingestion of radiopaque markers shows retention of markers in the rectosigmoid and descending colon.

Figure 3: In Figure 3A, an abdominal x-ray taken after colonoscopy with colonic manometry catheter placement shows the catheter coursing through the colon. An endoscopic clip attached to the catheter is visible in the proximal colon. In Figure 3B, the distal tip of the manometry catheter is visible extending down from the top of the image. A black suture has been tied to the tip of the catheter and an endoscopic clip is being placed to secure the catheter to the colonic mucosa.

We would like to thank Dr. Neetu Bali for these images.

Figure 4: In Figure 4A, a normal high-resolution colonic manometry tracing shows two series of high-amplitude propagating contractions that terminate near the anal canal, presumably in the area of the rectum. In Figure 4B, an abnormal colonic manometry tracing shows

multiple series of high-amplitude propagating contractions that terminate prematurely, approximately halfway through the studied colon.

Figure 5: An abdominal x-ray shows a sacral nerve stimulator lead and implanted pulse generator and battery.

Table 1: Dosing recommendations for commonly used oral and rectal laxatives. *Adapted with permission from Tabbers MM, et al. Evaluation and treatment of functional constipation in infants and children: evidence-based recommendations from ESPGHAN and NASPGHAN. Journal of pediatric gastroenterology and nutrition. 2014;58(2):258-74 (1).*

Medication	**Dosing recommendations**
Osmotic laxatives	
Lactulose	1-2 g/kg, once or twice per day
PEG 3350	Maintenance: 0.2-0.8 g/kg/day Fecal disimpaction: 1-1.5 g/kg/day (up to 6 consecutive days)
Milk of magnesia	2-5 years: 0.4-1.2 g/day, once or divided 6-11 years: 1.2-2.4 g/day, once or divided 12-18 years: 2.4-4.8 g/day, once or divided
Stool softeners	
Mineral oil	1-18 years: 1-3 ml/kg/day, once or divided, max 90 ml/day
Stimulant laxatives	
Bisacodyl	3-10 years: 5 mg/day >10 years: 5-10 mg/day
Senna	2-6 years: 2.5-5 mg once or twice per day 6-12 years: 7.5-10 mg/day >12 years: 15-20 mg/day
Rectal laxatives/enemas	
Bisacodyl	2-10 years: 5 mg once per day >10 years: 5-10 mg once per day
Sodium docusate	<6 years: 60 ml >6 years: 120 ml
Sodium phosphate	1-18 years: 2.5 ml/kg, max 133 ml/dose
Sodium chloride	Neonate <1 kg: 5 ml

	Neonate >1 kg: 10 ml 1-2 years: 6 ml/kg once or twice per day 2-11 years: 30-60 ml once per day >11 years: 60-150 ml once per day
Mineral oil	2-11 years: 30-60 ml once per day >11 years: 60-150 ml once per day

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